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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Carlsson et al.
Appl. No.	:	09/623,602
Filed	:	09/05/2000
Title	:	TOPICAL FORMULATION OF OIL-IN-WATER TYPE COMPRISING OF GALACTOLIPID MATERIAL AS EMULSIFIER, WITH A PROLONGED EFFECT OF AN INCORPORATED ACTIVE SUBSTANCE
Grp./A.U.	:	1616
Examiner	:	Gollamudi, Sharmila S.
Docket No.	:	13454NP

Honorable Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

RESPONSE TO OFFICIAL ACTION

In response to the non-final office action mailed September 4, 2002, applicants respectfully request reconsideration of the continued rejection of claims 1-13 for the reasons discussed below.

In the latest office action, claims 1-13 have been rejected under 35 U.S.C. 103(a) as being obvious and therefore unpatentable over US Patent 6,068,860 when considered in view of the teachings of WO Publication WO 95/20943.

In making the rejection, the Examiner has stated that the Carlsson et al., US patent reference, discloses pharmaceutical formulations which contain galactolipids and has cited, in particular, example 5 of the reference. Unlike the present

invention, the carrier disclosed and taught in the reference is a gel containing 40% of galactolipids and not an emulsion with an oil phase, as is the case with the present invention. Further, the intended use of the galactolipid materials in the cited references is not the same as is taught in the present invention.

In the US Patent 6,068,860 the problems to be solved by the invention are clearly outlined at column 3 beginning at line 43 of the patent. First, the patent seeks to bring a sufficient amount of an active substance to penetrate the stratum corneum rapidly. Secondly, the active substance must accumulate at a proper site, which is preferably in the living epidermis where replication of herpes viruses takes place. A further problem to be solved by the cited reference is the prevention of inflammation which may follow upon virus multiplication. It is noted that there is nothing in the teachings of the cited reference to the desirability of obtaining a prolonged effect of a pharmaceutically or cosmetically active substance when applied topically, as is the case with the present invention.

It has long been held that in order to support a combination rejection for obviousness, the primary reference must have a sufficient nexus to the invention as is claimed. In the present instance, applicants claim a method for prolonging a local effect of a pharmaceutically or cosmetically active substance when applied with a topical cream or lotion. The reference, however, is directed to providing a pharmaceutical composition which is

not irritating, which penetrates the skin rapidly and which provides for a target concentration of a pharmaceutical, such as foscarnet, at a predetermined area so as to sustain a high concentration of the pharmaceutical at the predetermined area. In effect, the cited references uses galactolipids with a polar solvent as a carrier in a composition to provide "a site-directed delivery of foscarnet to the living epidermis, thereby giving a maximum drug concentration at the site of disease with a minimum adverse effects." See column 4, lines 17-21.

In the cited reference, it is the ability to concentrate the pharmaceutical at a predetermine site without inflammatory reactions which is taught. There is no suggestion that a prolonged effect of a pharmaceutical agent is obtained in a manner as taught by the present application and as set forth in claims 1-13 of the present application. The ability of a formulation to provide a high concentration of an active would not suggest that one of ordinary skill in the art that a prolonged effect can be obtained by a topical application of a cream or lotion utilizing a galactolipid material as an emulsifier, as is specifically claimed in applicants claims 1-13.

The reference to the WO Publication has been cited as disclosing a topical oil-in-water emulsion containing galactolipids. The Examiner has further stated that the reference teaches that "an intrinsic beneficial feature of the galactolipids is the galactose units comprising the polar

headgroup in each lipid molecule, which may sterically stabilize the emulsion droplets, and thus provide for a prolonged life-span when injected into the blood stream." See page 5, lines 1-5 of the reference.

What has been cited as showing a prolonged effect, however, is directly referencing the fact that the life-span of emulsion droplets in the blood stream are prolonged due to the inherent properties of the galactolipid material. In other words, the droplets are preserved for a longer period time in an aqueous medium. There is nothing disclosed nor taught about effecting the behavior of any incorporated active substance.

In the present invention, however, there is specifically taught that there is a prolongation of the local effect of an active substance incorporated into a lipid carrier of an oil-in-water emulsion after application to the skin. After the application of a cream or lotion to the skin, the emulsion droplets are no longer present, as the emulsion has been broken down and the aqueous phase evaporated. It is submitted that the prolonged life-span of emulsion droplets in the blood stream, as taught in the WO Publication, would not teach one of ordinary skill in the art that an effect of an active substance in a topically applied cream or lotion could be prolonged. Further, there is no suggestion of providing an oil-in-water emulsion carrier, including an oily non-polar lipid material, an aqueous phase and a galactolipid material as an emulsifier, as is taught

in the present invention to prolong an effect of an active substance.

To further illustrate the distinction of what is taught in the WO publication and what is taught in the present application, one must also look to the use or intent of use of the formulations in the WO Publication. At page 6 of the reference, it is specifically noted that emulsions based on galactolipids are "surprisingly stable preparations compared to phospholipid emulsions..." Secondly, galactolipids emulsions "exhibit a narrow and consistent particle size distribution, which normally is a problem with phospholipid emulsions." And thirdly, galactolipid emulsions "are also surprisingly stable to sterilisation by autoclaving in a standard autoclave."

In view of the foregoing, what is fairly taught in the WO Publication is that the galactolipid emulsions are used in pharmaceutical compositions because they are stable when subjected to mechanical agitation or shaking. Further, that such emulsions provide a narrow and consistent particle-size distribution throughout the composition, and thirdly that the emulsions are stable under the application of heat, such as due to sterilization during autoclaving. Again, there is no suggestion that the galactolipid emulsions can be used in formulations to prolong the topical effect of active substances, as is taught in the present application.

The Examiner's attention is directed to the conclusions set

forth in the WO Publication at line 25 wherein the inventive intent for the use of a galactolipid emulsion is definitively set forth. As stated therein,

> "Our findings related to the invention are that it is possible to produce remarkably stable oil-in-water emulsions based on the galactolipid material, which fulfils the important and necessary requirements as being autoclavable and resistant to harsh mechanical treatments. The emulsions have particle size distributions which are suitable for parenteral and intravenous uses. The emulsions do not exhibit any unpleasant odour or taste and they are remarkably stable towards oxidation. This invention provides an alternative to the phospholipid emulsions which offers concrete advantages compared to such emulsions."

Concerning the specific combination rejection, it is not believed that one of ordinary skill in the art would look to the teachings of the WO Publication to modify the teachings of US Patent 6,068,860 because the specific inventive intent in the "860" patent is different than that as set forth in the WO Publication. In the "860" patent, it is the specific targeting and concentrating of a pharmaceutical at a predetermined site without inflammation which is the thrust of the invention. It is not seen how one of ordinary skill in the art would look to provide concentration by utilizing the compositions set forth in the WO Publication as the intent of the use of the galactolipid emulsifiers in the WO Publication as to provide stability, particle distribution and heat resistance. There is no suggestion or teaching that the emulsions in the WO Publication could or would effect concentration of a pharmaceutical at a

specific site which is the specific intent necessary in the "860" patent.

In view of the foregoing, it is respectfully submitted that neither of the primary references discloses a method of prolonging a local effect of a pharmaceutically or cosmetically active substance used in a topical cream or lotion after the cream or lotion is applied topically and wherein an oil-in-water emulsion is used as the carrier, with such emulsion including an oily non-polar lipid material, an aqueous phase and galactolipid material as the emulsifier.

The reference to Horrobin, US Patent 4,444,755, has also been considered, however, due to the differences between the primary references and the present invention, it is believed that the secondary reference does not add to the obviousness rejection. Further, this reference refers to the use of gamma-linolenic acid dihomogamma-linolenic acid or "physiologically functional derivatives thereof" for the treatment of skin disorders. However, in the present invention the active substance to be incorporated in the cream or lotion, as is described in claim 12, is 13-hydroxy-linolenic acid which has little resemblance with the fatty acids disclosed in the Horrobin reference.

In addition to the foregoing, it is respectfully submitted that applicants have determined and discovered a new use for an oil-in-water emulsion which includes a galactolipid material as

an emulsifier. It has long been held that a new and obvious use for a known material is patentable subject matter. As the primary two references cited do not suggest or disclose the use of an oil-in-water emulsion, including a galactolipid material as an emulsifier for the purpose of prolonging a local effect of a pharmaceutically or cosmetically active substance, it is respectfully submitted that these references have not recognized nor make obvious the use which has been discovered by the applicants of the present invention. Therefore, it is respectfully submitted that the present application defines a novel and patentably distinct invention not disclosed by the prior art and certainly not suggested therein. Therefore, favorable consideration and allowance of claims 1-13 is requested.

Should the Examiner have any further questions concerning the allowability of the claims, it is requested that the Examiner contact the undersigned attorney of record to further expedite the prosecution of this application.

Respectfully submitted,

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